

## Mindfulness Student Study (MSS): Health Economic Analysis Plan (HEAP)

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### 1. Trial overview:

Details for this overview are drawn from: Galante et al. (2016) and Galante et al. (2017)

Published protocol: Galante et al. (2016)

Trial registration: ACTRN12615001160527 (<https://goo.gl/4jbZhx>)

#### 1.1 Background and rationale

University students show elevated levels of stress. Although mental illness rates among first year students appear to be lower than those of the general population, they surpass general population rates when undergraduates get to their second year (Macaskill, 2013). Students report academic pressure as the biggest trigger of their mental health problems (Kerr, 2013). University Counselling Services in the UK have noted the constant increase in the proportion of students seeking help in recent years (Mair, 2016, Williams et al., 2015). At the University of Cambridge, 8.5% of the students required access to counselling in 2014. An effective preventative intervention is needed to help students cope more effectively with academic life and develop resilience.

Mindfulness interventions have been shown to reduce stress and prevent depression in clinical and non-clinical populations (Gotink et al., 2015, Kendrick and Peveler, 2010). Secular mindfulness training involves paying attention to the present moment on purpose and non-judgmentally (Kabat-Zinn, 1994). It is popular among students and increasingly used to support them in the UK (Mindfulness for Students website, 2016). However, there is little evidence on the effectiveness of offering mindfulness training to this population or of any adverse effects. Previous randomised trials assessing mindfulness for supporting university students generally suffer from small sample sizes, lack of follow-up, low methodological quality and poor reporting (Bamber and Kraenzle Schneider, 2016). One of the best quality (e.g. with sample size calculation on main outcome, prospective trial registration, and low attrition) studies available to date randomised 288 medical and psychology Norwegian students to mindfulness-based stress reduction or a waitlist, and found moderate post-intervention effects on psychological distress and subjective well-being (de Vibe et al., 2013). A recent systematic review which meta-analysed nine randomised and non-randomised studies found that mindfulness significantly reduced anxiety among university students ( $d=0.73$ ; 95% CI 1.00 to 0.45) (Regehr et al., 2013); to our knowledge, none of these studies included an economic evaluation. Further, these reviews and others fail to make a distinction between therapeutic and preventative interventions (such as the one being evaluated here). A good-quality and adequately

powered randomised evaluation including a wider spectrum of university students is needed to: confirm previous findings, extend the follow-up period and provide a more complete view of the potential impact (positive and negative) of the provision of mindfulness training on university student life.

### 1.2 Aims, objectives and hypothesis

This study aims to evaluate whether the provision of a mindfulness course to higher education students:

1. Helps them to manage stress during the examination period;
2. Improves their mental well-being and resilience to stress up to one year later;
3. Reduces their use of mental health treatment and support services;
4. Improves their engagement with student life, including their academic performance.

The main hypothesis is that the provision of mindfulness training will reduce students' psychological distress during the examination period in comparison with students who have not been offered this provision.

### 1.3 Trial design

A pragmatic randomised controlled evaluation with two parallel arms and a one-to-one allocation rate testing the superiority of mindfulness training provision to no provision. Students from the University of Cambridge were recruited in two terms, forming two cohorts: cohort 1 was recruited between 28/09/2015 and 09/10/2015 (beginning of Michaelmas term), and cohort 2 (beginning of Lent term) between 30/11/2015 and 15/01/2016. Date of registration determined a participant's cohort. Figure 1 shows the participant timeline, with specific dates given in Table 1. There were four points of data collection: baseline (T0, varied by cohort); post intervention delivery (T1 across both arms, varied by cohort); summer exam term (T2, the same across cohorts); and one year post baseline follow-up (T3, varied by cohort).

Consent was collected primarily collected electronically (739/750) but a small number of participants (11/750) provided manual consent (they completed a paper based consent form available at the information sessions run at the beginning of each term; the paper form also collected their email address). Once participants consented, they were emailed with a link to the online baseline questionnaire; those who completed the questionnaire were randomised: (i) to joining a mindfulness course during the term in which they were recruited plus mental health provision as usual (PAU); or (ii) to PAU alone. Simple randomisation was done remotely by the survey software (Qualtrics) using computer generated random numbers (the same software was used to collect all subsequent student reported outcomes). Participants were informed of their allocation upon completion of the baseline questionnaire. Within each cohort, the points of data collection (T0-T3) were used in both arms.

PAU comprises access to individual counsellors, mental health advisors and psychiatrists at the University of Cambridge Counselling Service (UCS), as well as access to welfare staff in the University colleges (this provision varies across colleges, but can include college nurse, counsellor, welfare officer or tutor) and National Health Services (NHS). Those allocated to PAU alone were offered a mindfulness course one year later, providing they were still students at the University at this time.

The mindfulness intervention was offered for two terms before study initiation; this allowed the intervention to become established before evaluating it, and provided feasibility and acceptability data.

### *1.3.1 Participants*

Participant eligibility criteria were unchanged from those used routinely by the UCS for mindfulness courses. They are all self-reported. Inclusion criteria:

1. Undergraduate or postgraduate University of Cambridge students in any year or course;
2. Who considered that they could realistically attend at least seven sessions of the course.

Exclusion criteria:

1. Currently suffering from severe periods of anxiety or depression;
2. Experiencing severe mental illness such as hypomania or psychotic episodes;
3. Following recent bereavement or major loss;
4. Experiencing any other serious mental or physical health issue that would impact on their ability to engage with the course.

Students were advised to contact the study team if they are unsure about their eligibility.

### *1.3.2 Intervention overview*

The eight-week mindfulness course is called 'Mindfulness Skills for Students'. It consists of a secular, group-based skills training programme based on the course book 'Mindfulness: A Practical Guide to Finding Peace in a Frantic World' (Williams and Penman 2011), and adapted for university students. This intervention aims to optimise experiences across a range of students and is not specifically developed for those students in clinical ranges.

The first session lasts for 90 minutes and the others run for 75 minutes. There are eight weekly sessions, all run by Dr Elizabeth English, an experienced and certified mindfulness teacher. Each session includes two mindfulness meditations, the first embedding the meditation that the students have practised at home throughout the week; the second, introducing them to the new meditation that they will practice at home in the coming week. There are also periods of reflection and inquiry, helping the students to understand the nature of mindfulness, to deepen their learning and embed it into their everyday lives. A few simple models are used and developed throughout the course, to give the students some theoretical understanding of the concepts developed experientially. As is usual in mindfulness programmes, each session also included interactive exercises, so that students share their experience and get to know each other throughout the course, building a sense of safety and community.

Before and after each class, students received an email from the mindfulness teacher. This reminded them of the themes covered in the previous class, and informed them of the topics coming up in the next class. These emails also included handy tips, poems and video clips. There was also a course handout available in hardcopy at each class that could also be downloaded via a link in the post-class email, which described the home practice for the coming week. The home practice time varied through the course, starting at 8 min, and increasing to about 15–25 min/week plus ongoing reflection through the day. It included meditations from the course book's compact disc and other mindfulness practices such as a mindful walk, mindful eating, habit breakers and so on. More practice was possible for those who wanted it, and students were encouraged not to miss a day, but rather to consider doing less on days when they were busy. A detailed intervention manual is available from Dr Galante ([mjg231@medschl.cam.ac.uk](mailto:mjg231@medschl.cam.ac.uk)).

Seven Mindfulness Skills for Students (MSS) courses ran in parallel during each term (which only last nine weeks in Cambridge) with up to 30 students each. Students chose a session time and day to attend each week but were encouraged to attend as many sessions as they could; where they could not make their usual session, they could attend an alternative session within the same week (session hopping). Students were contacted by email when they missed a session to check whether the absence related to a negative experience with mindfulness and, subsequently, to offer support.

As a pragmatic study, care was taken not to interfere with or modify routine practices for intervention delivery. Therefore, there were no ad hoc adherence optimisation procedures. Participants in the control group were guaranteed a space in the following year's mindfulness course and were requested to inform the research team should they decide to learn mindfulness elsewhere during the follow-up period.

### *1.3.3 Outcomes and data collection*

Several outcomes were measured and compared between mindfulness and control groups to assess the effects of the course. The primary outcome was a self-reported global measure of psychological distress assessed during the examination term, the most stressful period of Cambridge students' academic year. Secondary outcomes were exploratory assessments, intended to explore mindfulness' effects in more focused ways. Details about the full range of outcomes are given in Galante et al. (2016), Table 1.

Psychological distress was measured using the Clinical Outcomes in Routine Evaluation Outcome Measure (CORE-OM), a 34-item generic questionnaire which was designed to assess efficacy and effectiveness across multiple disciplines offering psychological therapies, and has been widely used with UK university students. It is scored on a five-point scale ranging from 0 (not at all) to 4 (most or all the time). The total score range is 0–136; this is usually divided by number of completed items to form a total mean score. A higher score means more distress. CORE-OM has good convergent validity, internal and test-retest reliability and sensitivity to change (Evans et al., 2002). CORE-OM was collected at each of the data collection points (T0-T3); **a comparison of CORE-OM between arms during the exam term (T2) was the primary outcome** (clinical effectiveness) measure.

Students' subjective well-being was assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS), a questionnaire that captures a broad conception of well-being. It consists of 14 items, each scored on a five-point scale ranging from 1 (none of the time) to 5 (all of the time). A higher score indicates higher wellbeing. The WEMWBS has good validity, internal consistency and test-retest reliability with a sample of UK students (n=354) and general population (n=2,075) (Tennant et al., 2007). WEMWBS was collected at each of the data collection points (T0-T3).

Mental health services use was assessed by asking students whether during the examination term they had requested help with mental health issues and stress from a range of resources (eg, psychiatrist, Samaritans). Participants were also asked to what extent such problems may have impacted on their academic performance (eg, 'To what extent do you have problems affecting your study?') and whether in their view their academic course workload was manageable. Data on inability to sit examinations was provided by the Student Registry. The UCS provided the research team with information about which participants used their services and how frequently they were used.

The following baseline data was also collected to compare the sample with the student population, and to run subgroup analyses: (1) students' prior experience with meditation and mindfulness; (2) demographic data provided by the student registry (eg, disability, ethnicity, socioeconomic classification). All baseline data was collected before randomisation.

Questionnaires were web-based.

#### *1.3.4 Statistical aspects: sample size and analysis*

The minimum sample size required was calculated to detect a 0.3 SD change in psychological distress with CORE-OM, the primary outcome. This change constitutes a small difference, but is reasonable for a relatively short mindfulness course, and attractive if this shift happens at a community rather than a clinical level (Huppert, 2009).

A study of a non-clinical sample (746 students from two UK universities plus a community sample of 360 people) found a mean total score of 0.76 points and a SD of 0.59 points (Core System Group, 2015). To detect a change of 0.3 SDs at  $p < 0.05$  with 90% power, 550 students (275 per arm) were estimated to be needed, allowing for 20% loss to follow-up as informed by previous studies (eg, *Warnecke et al. (2011)*).

The primary analysis consisted of an intention-to-treat (ITT) analysis comparing the primary outcome, CORE-OM during the examination period, between arms adjusted for baseline scores, routine demographics and timing of receipt of intervention relative to examinations (as some will have done the course during Michaelmas 2015 and others during Lent 2016). Multiple imputation (MI) was used since variables had less than <40% missing data, a pre-condition to ensure validity of imputations, and was applied only to variables with expected missing completely at random and missing at random patterns (ie, where there were no reasons to think that the pattern may be missing not at random). This imputation took account of other CORE-OM data points and routinely collected demographics. A per-protocol analysis (minimum dose assumed to be 50% attendance of sessions (Gu et al., 2015)) was also conducted excluding individuals in the control group who engaged in meditation elsewhere during the follow-up period preceding outcome measurement.

Where outcomes will be analysed at three time points (CORE-OM, WEMWBS and altruism, measured at post-intervention, examination period and one-year follow-up) they will be analysed using a repeated measures design with a treatment by time interaction term to study their trajectories through the academic year and to determine whether differences (ie, intervention effects) were consistent over time. [As of 05.12.2017, outcomes have not been analysed beyond two time points (eg Easter term and baseline), so a mixed model has not been needed.]

All statistical analyses were and will be conducted at an  $\alpha$ -level of  $p = 0.05$  (two-sided). Linear or linear mixed models have been and will be used, as appropriate, for the analyses. Assumptions were tested and diagnostic plots will be explored to assess model fit. Descriptive statistics for continuous variables were and will be summarised using mean/SD and median/IQR. Discrete variables have been summarised by proportions.

It was expected that the clustering effect (clustering within the MSS classes) would be negligible: although this was a group intervention, the work is highly personal, all the courses were taught by the same teacher, each course includes students from different colleges and courses, and the 'session hopping' option introduced variability. During preparation of the first manuscript Galante et al. (2017), intraclass correlations were computed to check this by analysing session attendance patterns to determine the extent of any clustering effect. The clustering effect was found to be

minimal and so was not adjusted for. Had one been present, it was intended to adjust for it using multi-level techniques.

#### 1.4 Ethics

Approval was been obtained from Cambridge Psychology Research Ethics Committee (PRE.2015.060).

#### 1.5 Sponsor and funding

Sponsor: University of Cambridge (16 Mill Lane, Cambridge, CB2 1SB)

This research was funded by the University of Cambridge Vice-Chancellor's Endowment Fund, the University Counselling Service and the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) East of England, at Cambridgeshire and Peterborough NHS Foundation Trust. Funders had no direct roles in study design, data collection, management, analysis, and interpretation of data, writing of the report, nor the decision to submit the report for publication.

#### 1.6 Trial progress

At the time of writing (25.01.2018), the following progress has been made on the project:

1. All participant provided data collection is complete: details of numbers recruited and data-collection figures are given in Figure 2.
2. A paper Galante et al. (2017) reporting the primary effectiveness analysis has been published by The Lancet Public Health.

## 2 Economic objective and context

This within-trial economic evaluation will use data from the full Mindful Student Study (MSS). Its objective will be to determine the cost-utility of providing a class-based mindfulness intervention (see Section 1.3.2 for details) compared with mental health provision as usual (PAU), to support university students' resilience to stress.

The costing perspective (see Section 16.4 for a definition) will be the costs to the University Counselling Service (UCS). In the base-case analysis (see Section 16.1 for a definition), we will consider the costs incurred from recruitment until the primary outcome time-point during the exam term (see Section 1.3.3, Table 1 and Figure 1 for details). The base-case benefits measure will be the (mental health specific) quality adjusted life years (QALYs) as calculated from the CORE-OM values (the primary outcome of the trial – see Section 1.3.3 for further detail).

With increasing student fees and costs in the UK, it is in the interest of both students and universities to find the most effective and cost-effective approaches to maximising student wellbeing to enable them to derive as much benefit as possible from their studies and university experience. As noted in Section 1.1, university counselling services, both in the UK and more widely, have noted a constant

increase in the proportion of students seeking help in recent years. Trials of mindfulness interventions among students have been limited and of varying quality, prompting the MSS (see Section 1.1). We are unaware of any economic evaluations among these trials. The limited number of economic evaluations among this group parallels the limited number of economic evaluations more generally among therapeutic uses of mindfulness, such as in the ‘third-wave cognitive behavioural therapies’ – see Feliu-Soler et al. (2017).

### 3 Data collection methods

As noted in Section 1.3, there are four points of data collection: baseline (T0, varied by cohort); post intervention delivery (T1 across both arms, varied by cohort); summer exam term (T2, the *same* across cohorts); and one year post baseline follow-up (T3, varied by cohort). The relationship between these time points and the cohorts is shown in Figure 1; the precise dates of data collection are given in Table 1. The primary effectiveness outcome was based on a comparison between arms of CORE-OM at T2: thus, our base-case analysis focuses on costs/outcomes between baseline (T0) and the exam term (T2); sensitivity analyses explore costs/outcomes costs between baseline (T0) and the one year follow-up (T3). Within each *cohort*, the periods of data collection (T0-T3) were the same for both *arms*.

With participants’ permission, the University Counselling Service (UCS) has provided details of all service activities to support study participants during the complete data collection period (eg from 28/09/2015 to 23/01/2017). This includes details of: type of activity (including whether individual or group based); date of activity; allocated length of face-to-face contact; and whether the participant attended. Using this data, we will calculate the number of each activity ‘consumed’ by each participant (this will include activities where participants have booked but do *not* attend, as the corresponding resources cannot be used by other students). There may be differences in the number of activities between *cohorts* due to the different data collection periods for each cohort: we will report each cohort’s activities usage separately and adjust for such differences in the subsequent analysis (see Section 7).

As part of the study, the number of students attending each session of each mindfulness course was collected; this number includes both participants *and* students attending the session who are *not* involved in the study. For study participants, we have details of which, and subsequently how many, sessions of mindfulness they attended.

Outcome measurements (eg CORE-OM) were self-completed online by students at several time-points (see Section 1.3.3).

### 4 Unit costs of resources

There are two broad resource areas to be costed: activities provided by the UCS and a course of mindfulness (the intervention). Given the costing perspective, we do not consider the typical annual costing resources (eg ‘PSSRU Unit Costs of Health and Social Care’ (Curtis and Burns, 2016)) to be appropriate; instead, unit costs will be determined locally and reported explicitly to ensure transparency and reproducibility.

Unit costs of providing service activities will be determined in consultation with the head of the UCS (Géraldine Dufour). Through discussion, we will identify the major resource components for each

activity (expected to primarily consist of meeting face-to-face with clients and any related time for preparation) and estimate the amount of resources typically used by UCS staff in delivering these activities (duration of face-to-face client contact is recorded, as outlined in Section 3). We expect such resources to primarily correspond to the use of staff time, which will be costed to include salary and on-costs. For group activities, we will divide the total cost of delivering the activity by the mean number of students booking such sessions (calculated from UCS administrative data).

Working from the design of the intervention (Section 1.3.2) and in consultation with appropriate members of the research team (PI – Peter Jones; study lead – Julieta Galante; head of UCS – Géraldine Dufour; mindfulness intervention teacher – Elizabeth English), resources used in the delivery of the mindfulness course will be determined. We expect the most significant resource to be the mindfulness teacher’s time in delivering the session, associated preparation and communicating with the students outside of the sessions. We will explore if other resources are also used (eg printing course materials etc). The mindfulness teacher’s time will be costed to include salary and on-costs. We will estimate the total costs for one course of mindfulness (eight sessions – see Section 1.3.2). With thirty students booking on to each course of mindfulness, we will work out the cost per student booking on to a course as the total cost of the course divided by thirty (even where a student attends none of the course, by the delivery of the programme, it is not possible to give their 'place' to another student).

The UCS does not incur a direct cost for room hire: for its counselling sessions, it has its own building; for the Mindfulness course, colleges provided rooms free of charge. Thus, given the costing perspective of ‘cost to the UCS’, room hire costs will not be included when producing the above unit costs.

By combining the levels of resource with the unit costs, we will estimate the total cost for items of resource use; these can be summed to estimate the total cost for each participant. Costs will be based on 2017/2018 levels in pound sterling.

## 5 Outcomes

The base-case for the economic evaluation will utilise (*mental health specific*) QALYs calculated from CORE-OM scores (the primary measure for the trial) to measure health gains in terms of survival (in years) weighted for health related quality of life. Consequently, the economic evaluation will be a cost-utility analysis. CORE-OM scores are collected online at four time points via the online survey Qualtrics software: baseline (T0); post the period in which the mindfulness classes are delivered (T1 - for both arms); examination period (T2); and one year follow-up (T3). The range of dates for each of these collection periods differs by cohort (except for T2 – the same examination period is used for both cohorts) and are detailed in Table 1. The base-case analysis will focus on costs/benefits between T0 and T2 to match the primary outcomes reported in Galante et al. (2017).

As noted by Mavranouzouli et al. (2013, p.381): ‘there are concerns that generic measures may lack sensitivity in capturing important elements of health-related quality of life (HRQoL), due to their focus on physical aspects of health (for example, 4 of 5 items of the EQ-5D capture physical aspects of HRQoL).’ Consequently, Mavranouzouli has developed a preference-based measure specific to mental health based on the CORE-OM as part of her doctoral thesis (Mavranouzouli, 2014): health states (CORE-6D) from CORE-OM are developed in Mavranouzouli et al. (2011) and a valuation of the



states was conducted in Mavranouzouli et al. (2013) using time trade-off (an example time trade-off question might be: “How many years of health at the current level would you be willing to trade for a year of perfect health?”). Steps for calculating the utility scores from CORE-OM item responses are given in Appendix 1 (Section 15).

We will use the SPSS code (converted to the statistical software R (R Core Team, 2017)) given in Mavranouzouli (2014, p.369-372) to calculate utilities from the CORE-OM values. From these utility values, total (mental health specific) QALYs will be calculated via the area under the curve approach, using linear interpolation between time points, without adjustment for baseline differences (adjustments are made later, as noted in Section 7 and advocated by Manca et al. (2005)).

## 6 Data cleaning procedures

In preparation for Galante et al. (2017) large proportions of the trial data have already undergone data cleaning and preparation. However, further plausibility checks will be conducted, including checking the range UCS activities (eg do any participants have an implausible number of counselling activities recorded?). Should implausible values be found, they will be queried with the study lead (Julieta Galante).

## 7 Analysis undertaken to estimate the incremental cost and incremental effect

The base-case economic evaluation will consist of an ITT analysis, conducted on costs (two elements: provision of student specific UCS services and the costs of delivering the mindfulness sessions) and QALYs. Analysis will be over the period between T0 (baseline) and T2 (exam term) – see Table 1. This duration is within one year, so no discounting (see Section 16.3 for a definition) will be applied. The base-case period was chosen to match the primary outcome analysis reported in Galante et al. (2017).

To address missing data, we will follow the guidance in Faria et al. (2014) and use multiple imputation if appropriate.

A seemingly unrelated regression model (SUR) will be used to estimate incremental cost and incremental QALYs. Both cost and QALY scores will be adjusted for participant age, gender and cohort of recruitment; QALYs will be further adjusted by baseline utility, in line with Manca et al. (2005). These adjustments accord with the primary analysis specified in the protocol (Galante et al., 2016) and reported in Galante et al. (2017). Further in line with these, adjustments for clustering within the intervention classes will *not* be conducted (since the ICC between classes was minimal – see Section 1.3.4 and Galante et al. (2017)). Analysis will be conducted within the statistical software R (R Core Team, 2017) version 3.4.3.

## 8 Interpretation of economic evaluation

Where an intervention has both lower mean costs and improved mean QALYs compared to the control, it is said to be ‘dominant’ and said to be cost-effective based on the available evidence. However, where an intervention is on average more effective and more costly, or less effective and less costly, it is not immediately clear which should be preferred. Should this occur, cost-effectiveness can be expressed in the form of an incremental cost-effectiveness ratio (ICER), estimated by dividing the incremental cost (cost of intervention – cost of control) by the incremental benefits (QALYs of intervention – QALYs of control) of the intervention compared to control. If the

mindfulness intervention is not dominant compared to PAU, we will calculate an ICER; in the base-case analysis, this would give the cost per additional (mental health) QALY.

Using the clinical cut-offs of the CORE-OM, we will also report the cost per case avoided.

Threshold analysis will be used to investigate what cost savings (eg reductions in visits to a college nurse or tutor) would be needed to offset the added costs of the mindfulness course.

## 9 Analysis of uncertainty in economic evaluation

The level of uncertainty associated with the decision regarding cost-effectiveness will be estimated using a cost-effectiveness acceptability curve (CEAC) (Fenwick et al., 2006). The CEAC estimates the probability of mindfulness+PAU being cost-effective at various levels of willingness to pay for additional QALYs (base-case analysis) – see Section 16.2 for a longer description.

## 10 Sensitivity analyses

A series of analyses will be undertaken to investigate how robust findings are to various assumptions:

1. Complete case<sup>1</sup> analysis – repeat the base case, but only including participants for whom we have complete data; investigates the impact of MI;
2. Per-protocol analysis – investigates how results differ if we only consider those attending at least 50% (4) of the mindfulness sessions;
3. Conduct evaluation at one year – extend the base-case analysis to include costs and benefits up to T3, investigating whether benefits continue beyond the examination term;
4. Conduct a cost-effectiveness analysis (CEA) for CORE-OM – as for the base-case, but measure benefits in terms of CORE-OM at T2 (e.g., calculate the cost per CORE-OM point);
5. Conduct a CEA for WEM-WBS – as for the base-case, but measure benefits in terms of WEM-WBS at T2 (e.g., calculate the cost per WEM-WBS point).

## 11 Reporting results

Results will be reported in accordance with the Drummond and Jefferson (1996) and CHEERS (Husereau et al., 2013) checklists for economic evaluations.

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<sup>1</sup> Here, a 'complete case' is defined as participant data that has no missing values on the variables used within the SUR outlined in Section 7.

## 12 References

- BAMBER, M. D. & KRAENZLE SCHNEIDER, J. 2016. Mindfulness-based meditation to decrease stress and anxiety in college students: A narrative synthesis of the research. *Educational Research Review*, 18, 1-32.
- CORE SYSTEM GROUP. 2015. *CORE system user manual* [Online]. Leeds: CORE System Group. Available: <http://www.coreims.co.uk/index.html> [Accessed 15 September 2015].
- CURTIS, L. & BURNS, A. 2016. *Unit Costs of Health and Social Care 2016*, Kent, University of Kent.
- DE VIBE, M., SOLHAUG, I., TYSSSEN, R., FRIBORG, O., ROSENVINGE, J. H., SORLIE, T. & BJORN DAL, A. 2013. Mindfulness training for stress management: a randomised controlled study of medical and psychology students. *BMC Med Educ*, 13, 107.
- DRUMMOND, M. F. & JEFFERSON, T. O. 1996. Guidelines for authors and peer reviewers of economic submissions to the BMJ. *BMJ*, 313, 275-283.
- EVANS, C., CONNELL, J., BARKHAM, M., MARGISON, F., MCGRATH, G., MELLOR-CLARK, J. & AUDIN, K. 2002. Towards a standardised brief outcome measure: psychometric properties and utility of the CORE—OM. *The British Journal of Psychiatry*, 180, 51-60.
- FARIA, R., GOMES, M., EPSTEIN, D. & WHITE, I. R. 2014. A Guide to Handling Missing Data in Cost-Effectiveness Analysis Conducted Within Randomised Controlled Trials. *Pharmacoeconomics*, 32, 1157-1170.
- FELIU-SOLER, A., CEBOLLA, A., MCCRACKEN, L. M., D'AMICO, F., KNAPP, M., LÓPEZ-MONTOYO, A., GARCÍA-CAMPAYO, J., SOLER, J., BAÑOS, R. M., PÉREZ-ARANDA, A., ANDRÉS-RODRIGUEZ, L., RUBIO-VALERA, M. & LUCIANO, J. V. 2017. Economic Impact of Third-Wave Cognitive Behavioral Therapies: A Systematic Review and Quality Assessment of Economic Evaluations in Randomized Controlled Trials. *Behavior Therapy*.
- FENWICK, E., MARSHALL, D. A., LEVY, A. R. & NICHOL, G. 2006. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. *BMC Health Services Research*, 6.
- GALANTE, J., DUFOUR, G., BENTON, A., HOWARTH, E., VAINRE, M., CROUDACE, T. J., WAGNER, A. P., STOCHL, J. & JONES, P. B. 2016. Protocol for the Mindful Student Study: a randomised controlled trial of the provision of a mindfulness intervention to support university students' well-being and resilience to stress. *BMJ Open* [Online], 6. Available: <http://bmjopen.bmj.com/content/6/11/e012300>.
- GALANTE, J., DUFOUR, G., VAINRE, M., WAGNER, A. P., STOCHL, J., BENTON, A., LATHIA, N., HOWARTH, E. & JONES, P. B. 2017. A mindfulness-based intervention to increase resilience to stress in university students (the Mindful Student Study): a pragmatic randomised controlled trial. *The Lancet Public Health*.
- GOTINK, R. A., CHU, P., BUSSCHBACH, J. J., BENSON, H., FRICCHIONE, G. L. & HUNINK, M. G. 2015. Standardised mindfulness-based interventions in healthcare: an overview of systematic reviews and meta-analyses of RCTs. *PLoS One*, 10, e0124344.
- GU, J., STRAUSS, C., BOND, R. & CAVANAGH, K. 2015. How do mindfulness-based cognitive therapy and mindfulness-based stress reduction improve mental health and wellbeing? A systematic review and meta-analysis of mediation studies. *Clin Psychol Rev*, 37, 1-12.
- HUPPERT, F. A. 2009. A New Approach to Reducing Disorder and Improving Well-Being. *Perspectives on Psychological Science*, 4, 108-111.
- HUSEREAU, D., DRUMMOND, M., PETROU, S., CARSWELL, C., MOHER, D., GREENBERG, D., AUGUSTOVSKI, F., BRIGGS, A. H., MAUSKOPF, J. & LODER, E. 2013. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ : British Medical Journal*, 346.
- KABAT-ZINN, J. 1994. *Wherever you go, there you are: mindfulness meditation in everyday life*, New York, Hyperion.

- KENDRICK, T. & PEVELER, R. 2010. Guidelines for the management of depression: NICE work? *Br J Psychiatry*, 197, 345-7.
- KERR, H. 2013. Mental Distress Survey Overview. NUS Services Limited.
- MACASKILL, A. 2013. The mental health of university students in the United Kingdom. *British Journal of Guidance & Counselling*, 41, 426-441.
- MAIR, D. 2016. The rise and rise of higher education and therapeutic culture. In: MAIR, D. (ed.) *Short-term counselling in higher education—context, theory and practice*. Abingdon: Routledge.
- MANCA, A., HAWKINS, N. & SCULPHER, M. J. 2005. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ*, 14, 487-96.
- MAVRANEZOULI, I. 2014. *The derivation of a preference-based measure for people with common mental health problems from the Clinical Outcomes in Routine Evaluation Outcome Measure (CORE-OM)*. PhD, University of Sheffield.
- MAVRANEZOULI, I., BRAZIER, J. E., ROWEN, D. & BARKHAM, M. 2013. Estimating a Preference-Based Index from the Clinical Outcomes in Routine Evaluation–Outcome Measure (CORE-OM): Valuation of CORE-6D. *Medical Decision Making*, 33, 381-395.
- MAVRANEZOULI, I., BRAZIER, J. E., YOUNG, T. A. & BARKHAM, M. 2011. Using Rasch analysis to form plausible health states amenable to valuation: the development of CORE-6D from a measure of common mental health problems (CORE-OM). *Qual Life Res*, 20, 321-33.
- MINDFULNESS FOR STUDENTS WEBSITE. 2016. *Mindfulness courses at UK Universities* [Online]. Available: <http://mindfulnessforstudents.co.uk/mindfulness-courses-at-uk-universities/> [Accessed 27 January 2016 2016].
- R CORE TEAM. 2017. *R: A language and environment for statistical computing*. [Online]. Vienna, Austria: R Foundation for Statistical Computing. Available: <http://www.R-project.org/>. [Accessed].
- REGEHR, C., GLANCY, D. & PITTS, A. 2013. Interventions to reduce stress in university students: a review and meta-analysis. *J Affect Disord*, 148, 1-11.
- TENNANT, R., HILLER, L., FISHWICK, R., PLATT, S., JOSEPH, S., WEICH, S., PARKINSON, J., SECKER, J. & STEWART-BROWN, S. 2007. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*, 5, 63.
- WARNECKE, E., QUINN, S., OGDEN, K., TOWLE, N. & NELSON, M. R. 2011. A randomised controlled trial of the effects of mindfulness practice on medical student stress levels. *Med Educ*, 45, 381-8.
- WILLIAMS, M., COARE, P., MARVELL, R., POLLARD, E., HOUGHTON, A.-M. & ANDERSON, J. 2015. Brighton: Institute for Employment Studies and Researching Equity, Access and Partnership.
- WILLIAMS, M. & PENMAN, D. 2011. *Mindfulness: a practical guide to finding peace in a frantic world*, UK, Hachette.
- YORK HEALTH ECONOMICS CONSORTIUM. 2016. *A Glossary of Health Economic Terms*. [Online]. York: York Health Economics Consortium. Available: [www.yhec.co.uk/glossary/](http://www.yhec.co.uk/glossary/) [Accessed 03.01.2018].

13 Tables

**Table 1:** Dates of: data-collection; and UCS use collection periods. Within each cohort, the dates of data collection (T0-T3) are the same for both arms.

|                    |  | <b>Cohort 1</b>          | <b>Cohort 2</b>          |
|--------------------|--|--------------------------|--------------------------|
| <b>Study dates</b> | Recruitment/baseline data collection (T0)                                  | 28/09/2015<br>09/10/2015 | 30/11/2015<br>15/01/2016 |
|                    | Mindfulness course<br>(only delivered to intervention arm)                 | 13/10/2015<br>03/12/2015 | 19/01/2016<br>10/03/2016 |
|                    | Post mindfulness-course data collection (T1)<br>(collected from both arms) | 26/11/2015<br>22/12/2015 | 03/03/2016<br>24/03/2016 |
|                    | <b>Primary outcome:</b><br>Examination period data collection (T2)         | 28/04/2016<br>08/06/2016 | 28/04/2016<br>08/06/2016 |
|                    | One year follow-up data collection (T3)                                    | 26/09/2016<br>11/10/2016 | 10/01/2017<br>23/01/2017 |

14 Figures

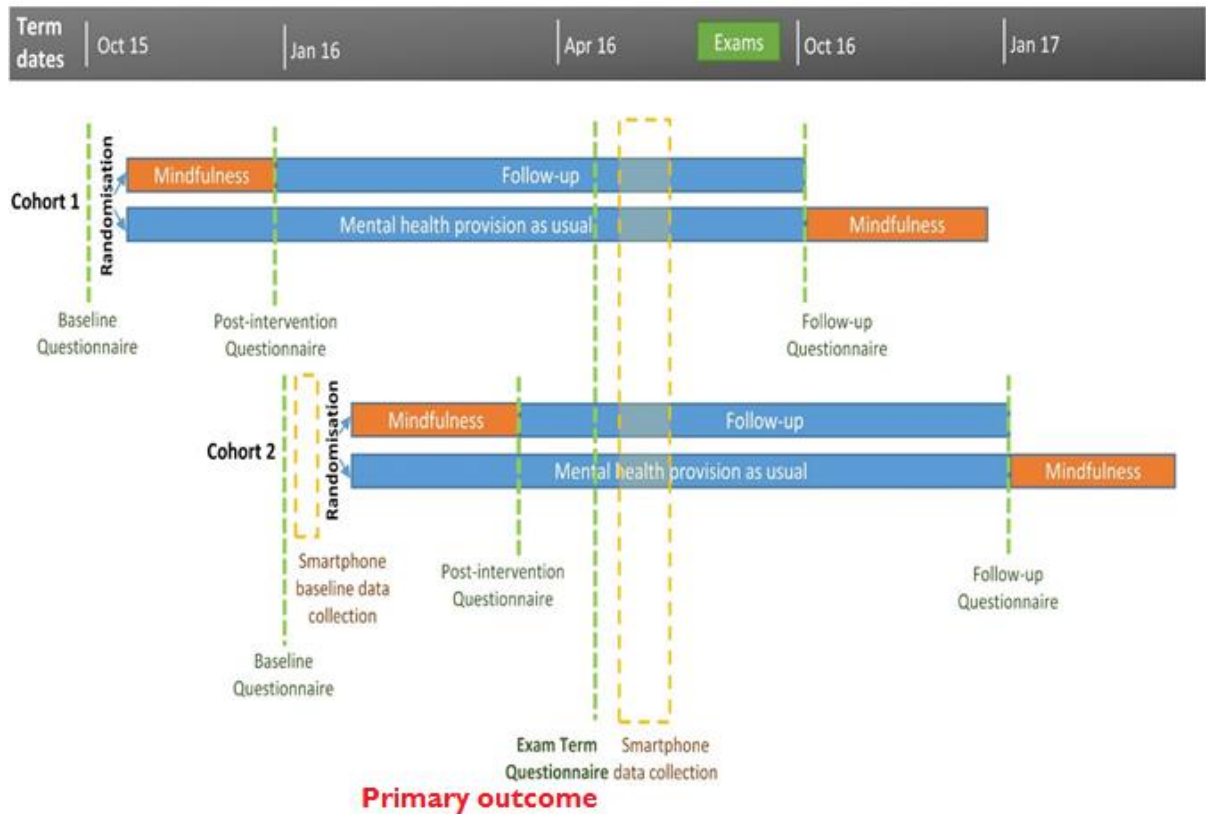


Figure 1. Participant timeline.

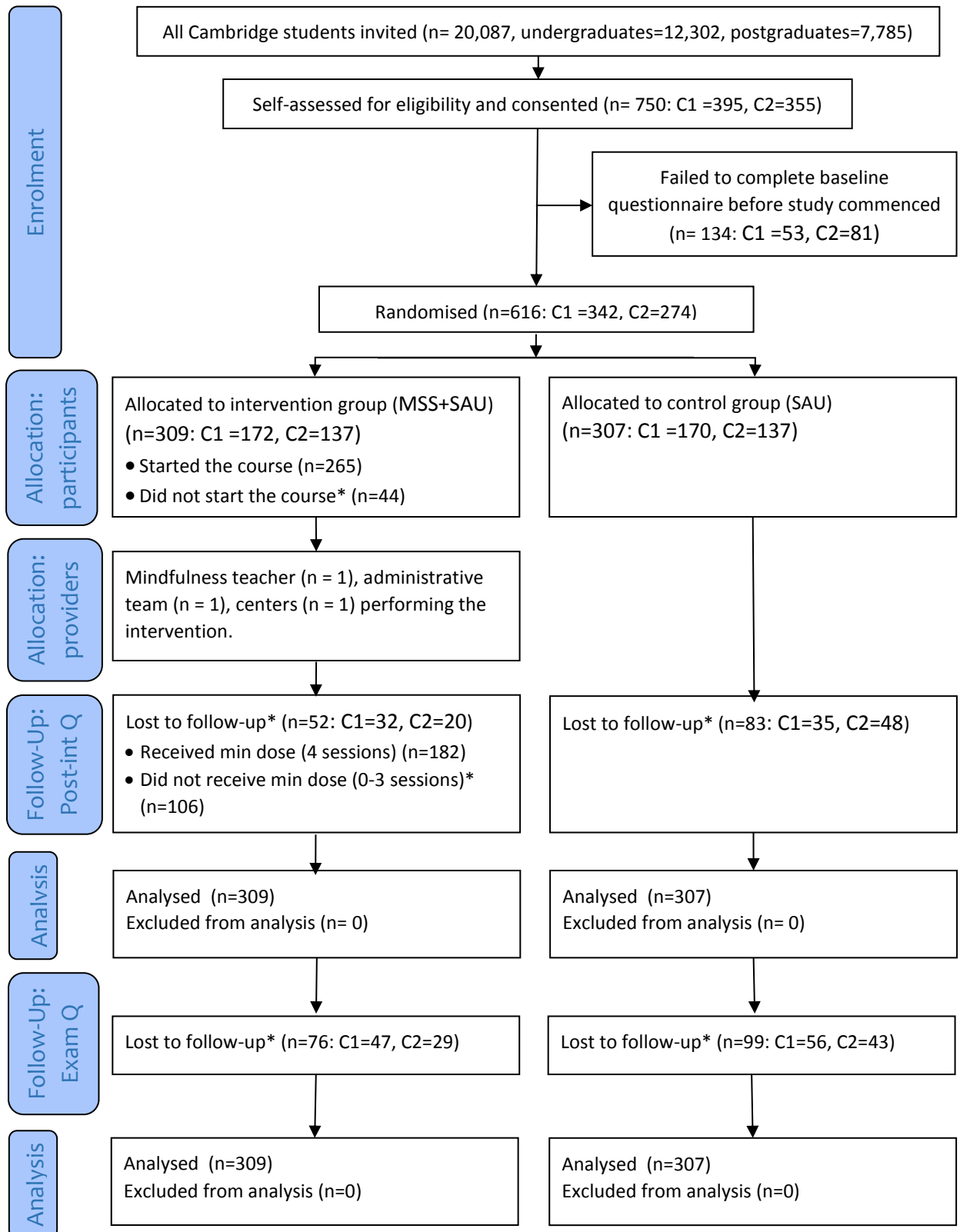


Figure 2. CONSORT 2010 flow diagram. \*Reasons explained in text. Abbreviations: C1: study cohort 1; C2: study cohort 2; post-int Q: ; min: minimum

### 15 Appendix 1: Calculating CORE-6D utility values from CORE-OM items

The details given here are based on Mavranouzouli et al. (2013) and Mavranouzouli (2014).

The utility score is based on CORE-OM items 1, 8, 15, 16, 21 and 33. These items are recoded as in Table A1 to form the CORE-6D (CO6D) items (*this table assumes that scores for item 21 have already been reversed*). The total score of the emotional component of the CORE-6D is given by the sum-score based on CORE-6D items 1, 15, 16, 21 and 33. The corresponding utility for each health state can then be determined from Table A2 using the emotional component score and responses to the physical item (recoded CORE-OM item 8).

Missing items on any of the underlying CORE-OM items (1, 8, 15, 16, 21 and 33) lead to a missing utility value.

**Table A1:** Conversion for taking CORE-OM items and forming CORE-6D items.

| CORE-6D component                |   | Emotional component |         |         |         |         | Physical item |
|----------------------------------|---|---------------------|---------|---------|---------|---------|---------------|
| CORE-6D (CO6D) item              |   | CO6D-1              | CO6D-15 | CO6D-16 | CO6D-21 | CO6D-33 | CO6D-8        |
| CORE-OM original item            |   | 1                   | 15      | 16      | 21      | 33      | 8             |
| CORE-OM original response levels | 0 | 0                   | 0       | 0       | 0       | 0       | 0             |
|                                  | 1 | 1                   | 1       | 1       | 0       | 1       | 1             |
|                                  | 2 | 1                   | 1       | 1       | 1       | 1       | 1             |
|                                  | 3 | 2                   | 2       | 2       | 1       | 2       | 2             |
|                                  | 4 | 2                   | 2       | 2       | 2       | 2       | 2             |

**Table A2:** Utility values for the CORE-6D health states indexed by the total value of the emotional component and CO-6D-8 values. Draws heavily on Table 8, p.391, Mavranouzouli et al. (2013).

| CORE-6D sum score of emotional component | Response level of CO6D-8 |      |      |
|--|--------------------------|------|------|
|  | 0                        | 1    | 2    |
| 0  | 0.95                     | 0.92 | 0.81 |
| 1  | 0.94                     | 0.90 | 0.80 |
| 2  | 0.87                     | 0.84 | 0.73 |
| 3  | 0.80                     | 0.77 | 0.66 |
| 4  | 0.72                     | 0.69 | 0.58 |
| 5  | 0.64                     | 0.61 | 0.50 |
| 6  | 0.55                     | 0.52 | 0.41 |
| 7  | 0.47                     | 0.43 | 0.32 |
| 8  | 0.38                     | 0.35 | 0.24 |
| 9  | 0.30                     | 0.26 | 0.16 |
| 10                                       | 0.24                     | 0.20 | 0.10 |

## 16 Appendix 2: Glossary of health economic terms

Definitions for some key health economic terms are given below; these are taken from York Health Economics Consortium (2016).

### 16.1 Base case analysis

A base case analysis usually refers to the results obtained from running an economic model with the most likely or preferred set of assumptions and input values. Sensitivity analyses may then be used to explore how the results deviate from those of the base case analysis when input values and/or modelling assumptions are altered.

'Reference case' (analysis) may be used as an alternative to base case analysis, especially where analysts are directed to a standard set of modelling assumptions by an HTA organisation such as NICE.

### 16.2 Cost-Effectiveness Acceptability Curve (CEAC)

The cost-effectiveness acceptability curve (CEAC) is a graph summarising the impact of uncertainty on the result of an economic evaluation, frequently expressed as an ICER (incremental cost-effectiveness ratio) in relation to possible values of the cost-effectiveness threshold. The graph plots a range of cost-effectiveness thresholds on the horizontal axis against the probability that the intervention will be cost-effective at that threshold on the vertical axis. It can usually be drawn directly from the (stored) results of a probabilistic sensitivity analysis. The CEAC helps the decision-maker to understand the uncertainty associated with making a particular decision to approve or reject a new health technology.

### 16.3 Discounting and the Discount Rate

Economic evaluations refer to a choice to be made between alternative interventions at a specific point in time, however the costs and health outcomes associated with each intervention occur at different points in time, present or future. Costs and health outcomes that are predicted to occur in the future are usually valued less than present costs, and so it is recommended that they be discounted in analysis. This is usually achieved by expressing the results as series (streams) of health outcomes and costs over time, applying a discounting factor to each value in the series and then aggregating to give a 'present value' of each stream. The discount factor increases over time, based on an underlying discount rate. NICE guidelines recommend that costs and health outcomes should be discounted at 3.5% per year. So 1 QALY (or £100) experienced/spent in year 2 would have a 'present' value of 0.965 QALY (£96.50) in year 1. For year 11 the present values would be 0.700 QALYs (£70.03). The choice of discount rate is of particular importance in preventive healthcare interventions: the use of a higher discount rate results in less value being attached to costs and health outcomes in the future.

### 16.4 (Costing) Perspective

The perspective is the point of view adopted when deciding which types of costs and health benefits are to be included in an economic evaluation. Typical viewpoints are those of the patient, hospital/clinic, healthcare system or society. The broadest perspective is societal', which reflects a full range of social opportunity costs associated with different interventions. In particular, this includes productivity losses arising from patients' inability to work, and changes in these losses associated with a new therapy. In its reference case NICE recommends a perspective of 'NHS and personal and social services', recognising that the societal perspective may bias against those not in work, such as people over retirement age or those not able to work due to health reasons. The NHS perspective includes treatment costs such as medicine costs, administration and monitoring, other health service resource use costs associated with the managing the disease (e.g. GP visits, hospital admissions), and costs of managing adverse events caused by treatment. It does not include patients' costs of obtaining care such as transportation, over-the-counter purchases, co-payments or time off work. For NICE's perspective on health outcomes, QALYs are based on the general population's valuation of health outcomes (obtained through surveys), and not patients own valuations of their health states.



## **Mindfulness Student Study (MSS): Amendments to Health Economic Analysis Plan (HEAP)**

Responsible health economist (HE): Adam P Wagner

Study lead: Dr Julieta Galante (PI: Prof Peter B Jones)

HE reviewer: Prof Garry Barton

Version: 1.0

### 1. Adjustments to “4. Unit costs of resources”

#### 1.1 Changes to costing UCS group activities

Subsequent discussions with the University Counselling Service (UCS) highlighted that there are two types of group activities offered by the UCS:

- Workshops: One-off sessions offered on a particular topic to a group of students.
- Groups: A series of sessions offered to a group of students. Should a student drop-out of a group, their place cannot be offered to another student.

When producing unit costs for Groups, we will cost attendance at the entire course of sessions.

The per-student cost of delivering Workshops or Groups will be determined by dividing the total cost of delivering the activity by the activity’s capacity (eg if an activity has a maximum capacity of four students, the per-student cost will be calculated as the total cost divided by four). This approach aligns with that proposed for costing the mindfulness course (total cost divided by 30, the capacity of the course). Activity capacity will be determined through consultation with the UCS.

#### 1.2 Costing year

The latest costing year for which data is available will be used.